

## SEQUENCE LISTING

<110> Hall, Roderick L. Poll, Christopher T. Newton, Benjamin B. Taylor, William J.A. <120> Method For Accelerating The Rate Of Mucociliary Clearance <130> 98-736-A <140> US 09/441,966 <141> 1999-11-17

<150> US 09/218,913 <151> 1998-12-22

<160> 106

<170> PatentIn version 3.1

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Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35 40

Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 70

Ser Ser Val Pro Ser Ala Pro Arg Gln Asp Ser Glu Asp His Ser

Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 105

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg

115 120 125

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 130 135 140

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Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly 50 55 60

Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala 65 70 75 80

Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala 85 90 95

Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp

100 105 . 110

His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala 115 120 125

Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val 130 135 140

Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn 145 150 155 160

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Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys 35 40 45

Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr Gly
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Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser Ala 65 70 75 80

Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr 85 90 95 Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser 100 Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe 120 Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu 135 Ala Cys Met Leu Arg Cys Phe Arg Gln 150 <210> 4 <211> 58 <212> PRT <213> Homo sapiens <400> 4 Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg Ala 10 Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln Leu 20 25 Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys 35 40 Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 50 <210> 5 <211> 51 <212> PRT <213> Homo sapiens <400> 5 Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly 20

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Lys Val Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn 35 40 45

Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly 50 55 60

Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala 65 70 75 80

Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala 85 90 95

Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp

100 105 110

His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala 115 120 125

Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val 130 135 140

Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn 145 150 155 160

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Asp Gly Ser Cys Gln Leu Phe Xaa Tyr Xaa Gly Cys Xaa Xaa Xaa Ser 35 40 45

Asn Asn Tyr Xaa Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Xaa 50 60

Thr Glu Asn Ala Thr Gly Asp Leu Ser Thr Ser Arg Asn Ala Ala Asp 70 75 80

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu His Asp Ser 85 90 95

Ser Asp Met Phe Asn Tyr Xaa Glu Tyr Cys Thr Ala Asn Ala Val Xaa 100 105 110

Gly Xaa Cys Xaa Xaa Xaa Xaa Xaa Trp Tyr Phe Asp Val Glu Arg

115 120

125

Asn Ser Cys Asn Asn Phe Xaa Tyr Xaa Gly Cys Xaa Xaa Xaa Lys Asn Ser Tyr Xaa Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Xaa Gln 150 Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Leu Ala Gly 170 165 Ala Val Ser <210> 12 <211> 393 <212> DNA <213> Homo sapiens <220> <221> misc\_feature (361)..(361) <222> <223> "n" is any nucleotide. <220> <221> misc feature (367)..(367) <222> <223> "n" is any nucleotide. <220> <221> misc feature <222> (384)..(384) <223> "n" is any nucleotide. <220> <221> misc\_feature <222> (390)...(390) <223> "n" is any nucleotide. <400> ggoogggtog tttctogect ggotgggatc getgeteete tetggggtee tggceggeeg 60 accgagaacg cagcatccac gacttctgcc tggtgtcgaa ggtggtgggc agattccggg 120 cctccatgcc taggtggtgg tacaatgtca ctgacggatc ctgccagctg tttgtgtatg 180 ggggctgtga cggaaacagc aataattacc tgaccaagga ggagtgcctc aagaaatgtg 240

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ccactgtcac agagaatgcc acgggtgacc tggccaccag caggaatgca gcggattcct
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Lys Val Val Gly Arg Phe Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn
Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly
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Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala
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Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser
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aaggcaggat totgaagaco actooagoga tatgttoaac tatgaagaat actgcacogo
caacgcagtc actgggcctt gccgtgcatc cttcccacgc tggtactttg acgtggagag
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                                                                      120
catgcctagg tggtggtaca atgtcactga cggatcctgc cagctgtttg tgtatggggg
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ctgtgacgga aacagcaata attacctgac caaggaggag tgcctcaaga aatgtgccac
                                                                      240
tgtcacagag aatgccacgg gtgacctggc caccagcagg aatgcagcgg attcctctgt
                                                                      300
cccaagtgct cccagaaggc aggattctga agaccactcc agcgatatgt tcaactatga
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                                                                       120
aatgtcactg acggatcctg ccagctgttt gtgtatgggg gctgtgacgg aaacagcaat
                                                                       180
aattacctga ccaaggagga gtgcctcaag aaatgtgcca ctgtcacaga gaatgccacg
                                                                       240
ggtgacctgg ccaccagcag gaatgcagcg gattcctctg tcccaagtgc tcccagaagg
                                                                       300
caggattctg aagaccactc cagcgatatg ttcaactatg aagaatactg caccgccaac
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Met Lys Arg Phe Phe Phe Asn Ile Phe Thr Arg Gln Cys Glu Glu Phe
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Ile Tyr Gly Gly Cys Glu Gly Asn Gln Asn Arg Phe Glu Ser Leu Glu
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Glu Cys Lys Lys Met Cys Thr Arg Asp
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Ile Thr Arg Tyr Phe Tyr Asn Asn Gln Thr Lys Gln Cys Glu Arg Phe
            20
                                25
                                                     30
Lys Tyr Gly Gly Cys Leu Gly Asn Met Asn Asn Phe Glu Thr Leu Glu
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Glu Cys Lys Asn Ile Cys Glu Asp Gly
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Pro Ser Trp Cys Leu Thr Pro Ala Asp Arg Gly Leu Cys Arg Ala Asn
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Glu Asn Arg Phe Tyr Tyr Asn Ser Val Ile Gly Lys Cys Arg Pro Phe
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Lys Tyr Ser Gly Cys Gly Gly Asn Glu Asn Asn Phe Thr Ser Lys Gln
                            40
Glu Cys Leu Arg Ala Cys Lys Lys Gly
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Kunitz-like domain of tissue factor pathway inhibitor precursor 2.

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Ala Cys Asp Asp Ala Cys Trp Arg Ile
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Asp Cys Lys Arg Ala Cys Ala Lys Ala
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<400> 23

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                                25
Ile Thr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Glu Ser Glu Asp
Tyr Cys Met Ala Val Cys Lys Ala Met
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Arg Ile Ile Arg Tyr Phe Tyr Asn Ala Lys Ala Gly Leu Cys Gln Thr
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Phe Val Tyr Gly Gly Cys Arg Ala Lys Arg Asn Asn Phe Lys Ser Ala
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Glu Asp Cys Met Arg Thr Cys Gly Gly Ala
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Gln Thr Cys
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Phe Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu

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Tyr Cys Met Ala Val Cys Gly Ser Ala
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<213> Unknown
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<223>
      Kunitz-like domain of collagen alpha-3(VI) precursor.
<400> 28
Cys Lys Leu Pro Lys Asp Glu Gly Thr Cys Arg Asp Phe Ile Leu Lys
                                    10
Trp Tyr Tyr Asp Pro Asn Thr Lys Ser Cys Ala Arg Phe Trp Tyr Gly
Gly Cys Gly Gly Asn Glu Asn Lys Phe Gly Ser Gln Lys Glu Cys Glu
Lys Val Cys
    50
<210> 29
<211>
      57
<212>
     PRT
<213> Unknown
<220>
<223> Kunitz-like domain of HKI-B9.
<400> 29
Pro Asn Val Cys Ala Phe Pro Met Glu Lys Gly Pro Cys Gln Thr Tyr
                5
Met Thr Arg Trp Phe Phe Asn Phe Glu Thr Gly Glu Cys Glu Leu Phe
Ala Tyr Gly Gly Cys Gly Gly Asn Ser Asn Asn Phe Leu Arg Lys Glu
                            40
                                               45
Lys Cys Glu Lys Phe Cys Lys Phe Thr
   50
```

<210> 30

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<212>
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<213>
      Artificial Sequence
<220>
<223>
      5' sense oligonucleotide used in Example 6.
<400> 30
gccaagcttg gataaaagat atgaagaata ctgcaccgcc aacgca
                                                                       46
<210>
      31
      35
<211>
<212>
      DNA
<213> Artificial Sequence
<220>
     3' antisense oligonucleotide used in Example 6.
<223>
<400> 31
                                                                       35
ggggatcctc actgctggcg gaagcagcgg agcat
<210>
      32
<211>
      206
<212>
      DNA
<213> Artificial Sequence
<220>
      Cloned bikunin cDNA fragment in Example 6.
<223>
<400> 32
ccaagettgg ataaaagata tgaagaatac tgcaccgcca acgcagtcac tgggccttgc
                                                                       60
cgtgcatcct tcccacgctg gtactttgac gtggagagga actcctgcaa taacttcatc
                                                                      120
tatggaggct gccggggcaa taagaacagc taccgctctg aggaggcctg catgctccgc
                                                                      180
tgcttccgcc agcagtgagg atcccc
                                                                      206
<210> 33
<211>
      28
<212> DNA
<213> Artificial Sequence
<220>
<223>
      3' PCR primer used to amplify EST R74593.
<400> 33
                                                                       28
cgaagcttca tctccgaagc tccagacg
<210>
      34
<211>
      31
```

<212>

<213>

DNA

Artificial Sequence

```
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<223> 5' PCR primer used to amplify EST R74593.
<400> 34
                                                                       31<sup>r</sup>
aggatctaga caataattac ctgaccaagg a
<210>
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<211>
       36
<212> DNA
<213> Artificial Sequence
<220>
      5' PCR primer used to amplify EST R35464.
<223>
<400> 35
                                                                       36
ggtctagagg ccgggtcgtt tctcgcctgg ctggga
<210>
       36
<211>
       19
<212>
      DNA
<213> Artificial Sequence
<220>
      5' PCR primer used to amplify EST R34808.
<400> 36
cacctgatcg cgagacccc
                                                                       19
<210>
       37
<211>
       19
<212> DNA
<213> Artificial Sequence
<220>
<223>
       Vector specific DNA sequencing primer (SP6).
<4Ó0> 37
                                                                       19
gatttaggtg acactatag
<210>
       38
<211>
       20
<212>
      DNA
<213> Artificial Sequence
<220>
<223> Vector specific DNA sequencing primer (T7).
<400> 38
taatacgact cactataggg
                                                                       20
<210> 39
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<211>
       22
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223>
       Gene specific DNA sequencing primer.
<400> 39
ttacctgacc aaggaggagt gc
                                                                        22
<210>
       40
<211>
       23
<212>
       DNA
<213> Artificial Sequence
<220>
      Gene specific DNA sequencing primer.
<223>
<400> 40
aatccgctgc attcctgctg gtg
                                                                        23
<210>
       41
<211>
       20
<212>
      DNA
<213>
      Artificial Sequence
<220>
<223>
       Gene specific DNA sequencing primer.
<400> 41
cagtcactgg gccttgccgt
                                                                        20
<210>
      42
<211>
       105
<212> DNA
<213> Artificial Sequence
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<223>
      5' sense oligonucleotide used in Example 5.
<400> 42
gaaggggtaa gcttggataa aagatatgaa gaatactgca ccgccaacgc agtcactggg
                                                                        60
ccttgccgtg catccttccc acgctggtac tttgacgtgg agagg
                                                                       105
<210>
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<211>
       129
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      DNA
      Artificial Sequence
<220>
<223> 3' antisense oligonucleotide used in Example 5.
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```
B6
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<400> cgcggat		tact	ggcgg	ga ag	gcago	ggag	g cat	tgcag	gcc	tcci	caga	ıgc (	ggtag	gctgti	t	60
cttatte	gccc	cggca	agcct	c c	ataga	itgaa	gti	tattg	cag	gagt	tcct	ct	ccac	gtcaa	a	120
gtacca	gcg															129
<210><211><212><213>	44 207 DNA Arti	ficia	al Se	eque	nce						-			·		
<220> <223>	Clon	ed b	ikuni	in f:	ragme	ent i	n E	xampl	.e 5							
<400> gaaggg	44 gtaa	gctt	ggata	aa aa	agata	atgaa	gaa	atact	gca	ccg	ccaac	gc (	agtca	actgg	9	60
ccttgc	gtg	catco	cttco	cc a	cgcto	ggtac	tt!	tgacg	tgg	agag	ggaac	tc	ctgca	aataa	C	120
ttcatc	atg	gagg	ctgc	g g	ggcaa	ataag	g aa	cagct	acc	gct	ctgag	ıga (	ggcct	gcat	9	180
ctccgcl	gct	tccg	ccagt	a g	ggato	cc										207
<210><211><212><213>	45 248 PRT Arti	ficia	al Se	eque	nce											
<220> <223>	EST	deri	ved o	cons	ensus	s seq	[uen	ce of	hun	nan I	Bikun	in	(Figs	3. 4D	and	4G).
<220> <221> <222> <223>	SIGN		<b>)</b>							•						
<400>	45															
Met Leu 1	ı Arg	Ala	Glu 5	Ala	Asp	Gly	Val	Ser 10	Arg	Leu	Leu	Gly	Ser 15	Leu		
Leu Lei	ı Ser	Gly 20	Val	Leu	Ala	Ala	Asp 25	Arg	Glu	Arg	Ser	Ile 30	His	Asp		
Phe Cys	Leu 35	Val	Ser	Lys	Val	Val 40	Gly	Arg	Cys	Arg	Ala 45	Ser	Met	Pro		
Arg Trp		Tyr	Asn	Val	Thr 55	Asp	Gly	Ser	Сув	Gln 60	Leu	Phe	Val	Tyr		

Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys 65 70 75 80

Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala 85 90 95

Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg
100 105 110

Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr 115 120 125

Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg 130 135 140

Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly
145 150 155 160

Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met 165 170 175

Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu Pro Leu Gly Ser 180 185 190

Lys Val Val Leu Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe 195 200 205

Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln 210 215 220

Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln 225 230 235 240

Leu Val Lys Asn Thr Tyr Val Leu 245

<210> 46

<211> 782

<212> DNA

<213> Homo sapiens

<400> 46

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atccgggtgg cacggaggaa ccaggagcgt gccctgcgca ccgtctggag cttcggagat

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120

780

782

Bb

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<211> 240

<212> PRT

<213> Homo sapiens

<220>

ga

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<223>

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Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 1 5 10 15

Leu Gly Ser Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
20 25 30

Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg 35 40 45

Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln 50 60

Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr

70

65

Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr 85 90 95

Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser 100 105 110

Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn 115 120 125

Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala 130 135 140

Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn 145 150 155 160

Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu 165 170 175

Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu 180 185 190

Pro Leu Gly Ser Lys Val Val Val Leu Ala Gly Leu Phe Val Met Val
195 200 205

Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala 210 215 220

Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Phe Gly Asp 225 230 235 240

<210> 48

<211> 1544

<212> DNA

<213> Homo sapiens

<220>

<221> misc feature

<222> (1358)..(1358)

<223> "n" is any nucleotide.

<400> 48

gcacgagttg ggaggtgtag cgcggctctg aacgcgctga gggccgttga gtgtcgcagg

Blo

cggcgagggc gcgagtgagg	agcagaccca	ggcatcgcgc	gccgagaagg	ccgggcgtcc	120
ccacactgaa ggtccggaaa	ggcgacttcc	gggggctttg	gcacctggcg	gaccctcccg	180
gagcgtcggc acctgaacgc	gaggcgctcc	attgcgcgtg	cgcgttgagg	ggcttcccgc	240
acctgatcgc gagaccccaa	cggctggtgg	cgtcgcctgc	gcgtctcggc	tgagctggcc	300
atggcgcagc tgtgcgggct	gaggcggagc	cgggcgtttc	tegecetget	gggatcgctg	360
ctcctctctg gggtcctggc	ggccgaccga	gaacgcagca	tccacgactt	ctgcctggtg	420
tcgaaggtgg tgggcagatg	ccgggcctcc	atgcctaggt	ggtggtacaa	tgtcactgac	480
ggatcctgcc agctgtttgt	gtatgggggc	tgtgacggaa	acagcaataa	ttacctgacc	540
aaggaggagt gcctcaagaa	atgtgccact	gtcacagaga	atgccacggg	tgacctggcc	600
accagcagga atgcagcgga	ttcctctgtc	ccaagtgctc	ccagaaggca	ggattctgaa	660
gaccactcca gcgatatgtt	caactatgaa	gaatactgca	ccgccaacgc	agtcactggg	720
ccttgccgtg catccttccc	acgctggtac	tttgacgtgg	agaggaactc	ctgcaataac	780
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atccgggtgg cacggaggaa	ccaggagcgt	gccctgcgca	ccgtctggag	ctccggagat	1020
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tggggaaggg aggggagact	atgtgtgagc	ttttttaaa	tagagggatt	gactcggatt	1140
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tggcagggat gggtttgctt	tggaaatcct	ctaggaggct	cctcctcgca	tggcctgcag	1260
tctggcagca gccccgagtt	gtttcctcgc	tgatcgattt	ctttcctcca	ggtagagttt	1320
tctttgctta tgttgaatto	cattgcctcc	ttttctcnat	cacagaagtg	atgttggaat	1380
cgtttctttt gtttgtctga	tttatggttt	ttttaagtat	aaacaaaagt	tttttattag	1440
cattctgaaa gaaggaaagt	aaaatgtaca	agtttaataa	aaaggggcct	tcccctttag	1500
aataaatttc cagcatgttg	ctttcaaaaa	aaaaaaaaa	aaaa		1544

<sup>&</sup>lt;210> 49

<sup>&</sup>lt;211> 252

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

<sup>&</sup>lt;220>

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180

190

185

Pro Leu Gly Ser Lys Val Val Val Leu Ala Gly Leu Phe Val Met Val
195 200 205

210 215 Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp 230 235 Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val Leu 245 <210> 50 <211> 146 <212> PRT <213> Homo sapiens <400> 50 Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg Ala Ser Met Pro Arg 5 10 Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly 25 20 Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln 70 75 Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys 90 95 Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp

100

115

Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala

110

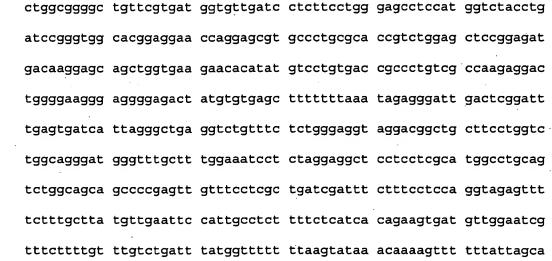
105

Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly

Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu

135

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Arg Cys
145
<210>
       51
       1530
<211>
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<213>
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<222>
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       "n" is any nucleotide.
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       misc_feature
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<223>
       "n" is any nucleotide.
<400>
      51
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                                                                        60
tegeaggegg egagggegeg agtgaggage agacceagge ategegegee gagaagnegg
gegteeccae actgaaggte eggaaaggeg actteegggg getttggeae etggeggaee
                                                                       180
ctcccggagc gtcggcacct gaacgcgagg cgctccattg cgcgtgcgtt tgaggggctt
                                                                       240
cccgcacctg atcgcgagac cccaacggct ggtggcgtcg ctgcgcgtct cggctgagct
                                                                       300
ggccatggcg cantgttgcg ggctgaggcg gacggcgttt ctcgcctgct gggatcgctg
                                                                       360
ctcctctctg gggtcctggc ggccgaccga gaacgcagca tccacgactt ctgcctggtg
                                                                       420
tcgaaggtgg tgggcagatg ccgggcctcc atgcctaggt ggtggtacaa tgtcactgac
                                                                       480
                                                                       540°
ggatcctgcc agctgtttgt gtatgggggc tgtgacggaa acagcaataa ttacctgacc
                                                                       600
aaggaggagt gcctcaagaa atgtgccact gtcacagaga atgccacggg tgacctggcc
accagcagga atgcagcgga ttcctctgtc ccaagtgctc ccagaaggca ggattctgaa
                                                                       660
gaccacteca gegatatgtt caactatgaa gaatactgca cegecaacge agteactggg
                                                                       720
cettgeegtg cateetteec acgetggtae tttgaegtgg agaggaacte etgeaataac
                                                                       780
```



ttctgaaaga aggaaagtaa aatgtacaag tttaataaaa aggggccttc ccctttagaa

ttcatctatg gaggctgccg gggcaataag aacagctacc gctctgagga ggcctgcatg

ctccgctgct tccgccagca ggagaatcct cccctgcccc ttggctcaaa ggtggtggtt

840

900

960

1020

1080

1140

1200

1260

1320

1380

1440

1500

1530

36

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<211> 170

<212> PRT

<213> Homo sapiens

taaaaaaaaa aaaaaaaaaa aaaaaaaaaa

<400> 52

Ala Asp Arg Glu Arg Ser Ile His Asp Phe Cys Leu Val Ser Lys Val 1 5 10 15

Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr 20 25 30

Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35 40 45

Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 50 55 60

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 65 70 75 80

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser 85 90 95 Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 105 110

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 115 120 125

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 130 135 140

Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln 145 150 155 160

Bb

Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys 165 170

<210> 53

<211> 27

<212> PRT

<213> Homo sapiens

<400> 53

Met Ala Gln Leu Cys Gly Leu Arg Arg Ser Arg Ala Phe Leu Ala Leu 1 5 10 15

Leu Gly Ser Leu Leu Ser Gly Val Leu Ala 20 25

<210> 54

<211> 23

<212> PRT

<213> Homo sapiens

<400> 54

Met Leu Arg Ala Glu Ala Asp Gly Val Ser Arg Leu Leu Gly Ser Leu 1 5 10 15

Leu Leu Ser Gly Val Leu Ala 20

<210> 55

<211> 102

<212> DNA

<213> Artificial Sequence

<220>

<223>	5' sense oligonucleotide used for construct #2 in Example 5.					
<400>	55					
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tgtaga	gctt cttttccaag atggtacttt gatgttgaaa ga	102				
<210>	56					
<211>	129					
<212>	DNA					
<213>	Artificial Sequence					
<220>	21 articopes alignment destricts used for sometiment #2 in Brownla	_				
<223>	3' antisense oligonucleotide used for construct #2 in Example	5.				
<400>	56					
	tect cattggegaa aacateteaa catacagget tetteagate tgtaagaatt	60				
55						
tttatt	acct ctacaaccac cgtaaataaa attattacaa gaatttcttt caacatcaaa	120				
gtacca	tat	129				
gcacca		129				
<210>	57					
<211>	108					
<212>						
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<220>						
<223>	5' sense oligonucleotide used for construct #3 in Example 5.					
100,5	bonne official about for competate #5 in fixample 5.					
<400>	57					
gaaggg	gtaa gettggataa aagaaattae gaagaataet gtaetgetaa tgetgttaet	60				
ggtcca	tgta gagcttcttt tccaagatgg tactttgatg ttgaaaga	108				
		•*				
<210>	58					
<211>	117					
<212>	DNA					
<213>	Artificial Sequence					
<220> <223>	El gongo eligenuglectide uged for geneturet #4 in Branche E					
<223>	5' sense oligonucleotide used for construct #4 in Example 5.					
<400>	58					
	gtaa gcttggataa aagagatatg tttaattacg aagaatactg tactgctaat	60				
gctgtt	actg gtccatgtag agcttctttt ccaagatggt actttgatgt tgaaaga	117				
<210>	59					
<211>						
<212>						

Artificial Sequence

```
<220>
     Sense oligonucleotide used in PCR in Example 8.
<223>
<400> 59
                                                                      19 -
cacctgatcg cgagacccc
<210> 60
<211>
      23
<212> DNA
<213> Artificial Sequence
<220>
      Antisense oligonucleotide used in PCR in Example 8.
<223>
<400> 60
                                                                      23
ctggcggaag cagcggagca tgc
<210>
      61
<211>
      45
<212> DNA
<213> Artificial Sequence
<220>
      Oligonucleotide used in in vitro mutagenesis in Example 9.
<223>
cgcgtctcgg ctgacctggc cctgcagatg gcgcacgtgt gcggg
                                                                      45
<210> 62
<211> 60
<212> DNA
<213> Artificial Sequence
<220>
      Oligonucleotide used in in vitro mutagenesis in Example 9.
<400> 62
ctgccccttg gctcaaagta ggaagatctt cccccgggg gggtggttct ggcggggctg
<210>
      63
<211>
      14
<212>
      PRT
<213> Homo sapiens
<400> 63
Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Pro Leu Gly
<210>
      64
<211>
      20
<212>
      PRT
```

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<213> Homo sapiens
<400> 64
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                                   10
Val Gly Arg Cys
<210> 65
<211>
      20
<212> PRT
<213> Homo sapiens
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Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys
                                   10
Arg Ala Ser Phe
       . 20
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<211> 11
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<213> Homo sapiens
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Pro Arg Tyr Val Asp Gly Ser Gln Phe Tyr Gly
               5
                                   10
<210> 67
<211> . 55
<212> PRT
<213> Homo sapiens
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Val Val Leu Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu
Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu
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Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu

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Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu
Arg Ala Leu Arg Thr Val Trp Ser Phe Gly Asp
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Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln GIu
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Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu
Val Lys Asn Thr Tyr Val Leu
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Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35 40 45

Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 50 55 60

Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 65 70 75 80

Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser 85 90 95

Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr
100 105 110

Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 115 120 125

Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 130 135 140

Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln 145 150 155 160

Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Leu Ala Gly 165 170 175

Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr 180 185 190

Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val
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Trp Ser Phe Gly Asp 210

<210> 71

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<212> PRT

<213> Homo sapiens

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- Val Gly Arg Cys Arg Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr
  20 25 30
- Asp Gly Ser Cys Gln Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser 35 40 45
- Asn Asn Tyr Leu Thr Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val 50 55 60
- Thr Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp 65 70 75 80
- Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser 85 90 95
- Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr 100 105 110
- Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg 115 120 125
- Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn 130 135 140
- Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln 145 150 155 160
- Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Leu Ala Gly 165 170 175
- Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr 180 185 190
- Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val 195 200 205
- Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val 210 215 220

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Leu
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Xaa Thr Xaa
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Pro Gly His Gln Glu Cys Ser Gly Phe Leu Cys Pro Lys Ser Pro
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                                    10
Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn Tyr Glu
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Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala Ser Phe
                            40
Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn Phe Ile
                                           60 ·
                        55
Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu Glu Ala
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65
Cys Met Leu Arg Cys Phe Arg Gln Glu Asn Pro Pro Leu Pro Leu
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Gly Ser Lys Val Val Leu Ala Gly Ala Val Ser
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                                                                      120
gaaggcagga ttctgaagac cactccagcg atatgttcaa ctatgaagaa tactgcaccg
                                                                      180
ccaacgcagt cactgggcct tgccgtgcat ccttcccacg ctggtacttt gacgtggaga
                                                                      240
ggaactectg caataactte atetatggag getgeegggg caataagaac agetaeeget
                                                                      300
ctgaggaggc ctgcatgctc cgctgcttcc gccagcagga gaatcctccc ctgccccttg
                                                                      360
gctcaaaggt ggtggttctg gccggggctg tttcgtgatg gtgttgatcc ttttcctggg
                                                                      420
gagentecat ggtettactg atteegggtg geaaggagga accaggageg tgeeetgegg
                                                                      480
ancgtctgga gcttcggaga tgacaagggn t
                                                                      511
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       in Fig. 3.
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Glu Glu Pro Gly Ala Cys Pro Ala Xaa Arg Leu Glu Leu Arg Arg

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gtcgcaggcg gcgagggcgc gagtgaggag cagacccagg catcgcgcgc cgagaagncg
                                                                      120
ggégtececa cactgaaggt eeggaaagge gaetteeggg ggetttggea eetggeggae
                                                                      180
cctcccggag cgtcggcacc tgaacgcgag gcgctccatt gcgcgtgcgt ntgaggggct
                                                                      240
tecegeacet gategegaga ecceaaegge tggtggegte geetgegegt eteggetgag
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ctggncatgt cg
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                                                                     120
gentececae actgaaggte eggaaaggeg actteegggg getttggeae etggeggaee
                                                                     180
ctcccggagc gtggcacctg aacgcgaggc gctccattgc gcgtgcgttt gaggggcttc
                                                                     240
ccgcacctga tcgcgagacc ccaacggctg gtggcgtcgc ctgcgcgtct cggctgagct
                                                                     300
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ggccatggcg cactgtgcgg ngctgaggcg
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                                                                     120
ggcggaccct cccggagcgt cggcacctga acgcgaggcg ctccattgcg cgtgcgtttg
aggggettee egeacetgat egegagaeee caaeggetgg tngegteget negegteteg
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gctgagcttg gccatggcgc antgttncgg gctnaggcgg acg
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(114)..(114)

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                                                                      120
tececacact gaaggteegg aaaggegaet teeggggget ttggcacetg geggaegtee
                                                                      180
cggagcnggc acctgaacgc gaggcgctcc attgcgcgtg cgtttgaggg gcttcccgca
                                                                      240
cetgategeg agaceceaac ggetggtnge gtegetggeg egttetegge tgagetggee
                                                                      300
atggcgcant gttgcgngct gaggcggacc gncgtttttc ttcgccttgc tgggattcgc
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ttgcttcctn tctgggggtt cctgggcggc cgaccgagaa cgcagcatcc aagaattttt
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423

gcc

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acgcgag	ggcg	ctccattgcg	cgtgcgtntg	gaggggcttc	ccgcacctga	tcgcgagacc	180
ccaacg	gctg	gtgggcgtcg	ctgcgcgtct	tcggctgagc	tgggccatgg	cgcanttgtt	240
gcgggct	tgag	gcggacgcgg	ncgtttttc	gnccttgctg	ggattcgttg	ttnctctctn	300
ggggtt	ctgg	ggnggccgan	cgagaacgca	agcattcacg	attt		344
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	m.!	. forture					
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		3)(233)					
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agctggccat ggcgcantgt tgcgngctga ggcggcggnc gttttctcgc ctgctgggat

cgctgc	tcct	ctctggggtc	ctggcggccg	accgagaacg	cagcatccac	ganttettee	24
tggtgt	tcga	agg					25
<210><211><211><212><213>	419 DNA	o sapiens					
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gaaaggo	cgac	ttccgggggc	tttggcacct	ggcggaccct	cccggagcgt	cggcacctga	180
acgcgag	ggcg	ctccattgcg	cgtgcgtttg	aggggcttcc	cgcacctgat	cgcgagaccc	240
caacgg	ctgg	tggcgtcgcc	tgcgcgtctc	ggctgagctg	gccatggcgc	antggtgcgg	300
gcttgag	ggcg	gannngccgt	ttctcgcctg	ctgggatcgc	tgctcctctc	tggggtcctg	360
gcggccg	gacc	gagaacgcag	catccacgac	ttctgcctgg	tgtcgaaggt	ggtgggcag	419

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                                                                      120
cctccattgc cgtgcgttng aggggcttcc cggaacttga tcgcgagacc ccaacggctg
                                                                      180
gtggcgtcgc tgcgcgtcct cggctgagct ggccatggcg cantggtgcc gngctgaggc
                                                                      240
eggagggeeg gtttetegee ttgetgggat egetgeteet etetggggte etggeggeeg
                                                                      300
ancgaagaan gcagcaatcc angaattnct gcctggtgtt cgaaagttgg tgggcanatt
                                                                      360
ccggggcctt catgnctaag gttggttggt anaatgtnaa ttaangattc ttgcaactgt
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                                                                       60
accgagaacg cagcatccac gacttctgcc tggtgtcgaa ggtggtgggc agattccggg
                                                                      120
cctccatgcc taggtggtgg tacaatgtca ctgacggatc ctgccagctg tttgtgtatg
                                                                      180
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240

300

ggggctgtga cggaaacagc aataattacc tgaccaagga ggagtgcctc aagaaatgtg

ccactgtcac agagaatgcc acgggtgacc tggccaccag caggaatgca gcggattcct

ctgtcc	caag tgctcccaga	aggcaggatt	cttgaagacc	acttcagcga	tatgtttcaa	. 360
ntattgr	naag aataattgca	ccgncaacgn	att		·	393
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catgcct	agg tggtggtaca	atgtcactga	cggatcctgc	cagctgtttg	tgtatggggg	180
ctgtgad	egga aacagcaata	attacctgac	caaggaggag	tgcctcaaga	aatgtgccac	240
tgtcaca	agag aatgccacgg	gtgacctggc	caccagcagg	aatgcagcgg	attcctctgt	300
cccaagt	gct cccagaaggc	aggattctga	agaccactcc	agcgatatgt	tcaactatga	360
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caatgtcact gacggatcct gccagctgtt tgtgtatggg ggctgtgacg gaaacagcaa
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taattacctg accaaggagg agtgcctcaa gaaatgtgcc actgtcacag agaatgccac
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gggtgacctg gccaccagca ggaatgcagc ggattcctct gtcccaagtg ctcccagaag
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gcaggattct gaagaccact ccagcgatat gttcaactat gaagaatact gcaccgccaa
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ctctgtccca agtgctccca gaaggcagga ttctgaagac cactccagcg atatgttcaa
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ctatgaagaa tactgcaccg ccaacgcagt ncactgggcc ttgcgtggca tnccttccca
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cgctngtact ttgacgtgga gaggaactcc tggcaataac ttcatctatg gaggcttgcc
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                                                                      120
                                                                      180
aaggcaggat totgaagaco actocagoga tatgttcaac tatgaagaat actgcacogo
caacgcagtc actgggcctt gccgtgcatc cttcccacgc tggtactttg acgtggagag
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gaactcctgc aataacttca tctatggagg ctgccggggc aataagaaca gctaccgctc
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293

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tccgggtggc acggaggaac ccaggancgt gccctgcgca ccgtctggag ctccggagat
                                                                     180
gacaaggagc agctggtgaa gaacacatat gtcctgtgac cgccctgtcg ccaagaggac
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                                                                      120
                                                                      180
gagaateete eeetgeeeet tggeteaaag gtggtggtte tggegggget gttegtgatg
gtgttgatcc tcttcctggg agcctccatg gtntacctga tccgggtngc acggaggaac
                                                                      240
                                                                      300
cagggagcgt gccctgcgna ccgtctngga gctccggaga tgacaaggag cagctggtga
agaacacata tgtcctgtga ccgncctgtt cgncaagagg actnggggaa aggggagggg
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teegggtgge aeggaggaac eagggagegt geeetgegea eegtetggga geteeggaga
                                                                      240
tgacaaggga gcagctggtg aagaacacat atgttcctgt tgaccgccct gttcgccaag
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agggantggg ggaaggggag ggggaganta ttgttgttga gntttttttt aaaattagga
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catggtctac ctgatccggg tngcacggag gaaccaggag cgtgccctgc gcaccgtctg
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gageteegga gatgacaagg ageagetggt gaagaacaca tatgteetgt gacegeeetg
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tcgccaagag gactggggaa gggaggggag actatgtgtg agctttttt aaatagaggg
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gaagggaggg gagactatgt gtgagctttt tttaaataga gggattgact cggatttgag
                                                                       240
tgatcattag ggctgaggtc tgtttctctg ggaggtagga cggctgcttc ctgggtcttg
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gcagggatgg ggtttgcttt gggaaatcct cttnggaggc tcctccttcg catgggcctt
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gcagtctngg cagcancccc cgagtttttt tccttcgctg atccgatttc ttttcctcca
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gagactatgt gtgagctttt tttaaataga gggattgact cggatttgag tgatcattag
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ttgctttgga gaatcctcta ngaggctcct cctcgcatgg cctgcagtct ggcagcagcc
                                                                       300
ccgagttgtt tcctcgctga tcgatttctt tcctccaggt agagttttct ttgcttatgt
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cageceegag tigtiteete getgategat tiettieete eaggtagagt titetitiget
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tatgttgaat tccattgcct cttttctcat cacagaagtg atgttggaat cgtttctttt
                                                                       240
gtttgtctga tttatggttt ttttaagtat aaacaaaagt tttttattag cattctgaaa
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tegeatggee tgeagtetgg cageageeee gagttgttne etegetgate gatntettte
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ccccaggtag agttttcttt gcttatgttg aantccattg cctcttttct catcacagaa
                                                                       240
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                                                                       300
agttttttat tagcattctg aaagaaggaa agtaaantgt acaagtttaa taaaaagggg
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DNA

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tegeatggee tgeagtetge ageageeeeg agttgtttee tegetgateg atttetttee
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tccaggtaga gttttctttg cttatgttga attccattgc ctctttctc atcacagaag
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gttttttatt agcattctga aagaaggaaa gtaaaatgta caagtttaat aaaaaggggc
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cncatcacag aagtgatgtt ggaatcgttt cttttgtttg tctgatttat ggttttttta
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240

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aataaaa	aagg	ggccttcccc	tttagaataa	aaaaaaaaa	aaaaaaaa		289
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			tgttgaattc				180
3-5-			-50544000			~~~~~~~~~~	100

tgttggaatc gttt	cttttg tttgtctgat	ttatggtttt	tttaagtata	aacaaaagtt	240
ttttattagc atto	tgaaag aaggaaagta	aaatgtacaa	gtttaataaa	aaggggcctt	300
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